the association and is required for said association of said first polypeptide and said second, binding partner polypeptide, and wherein said covalent modification comprises one of the group consisting of phosphorylation, acylation, geranylation, glycosylation, ubiquitination, prenylation, sentrinization, ADP-ribosylation and the reversal of these covalent modifications;

b) immobilizing the first polypeptide to a physical support;

c) contacting the immobilized polypeptide with the second, binding partner polypeptide;

d) contacting said immobilized polypeptide and said second, binding partner polypeptide with said sample; and

e) measuring the association of the second, binding partner polypeptide to the first polypeptide, thereby determining the covalent modification of at least one of said polypeptides, whereby the presence of a modifying enzyme is detected.

17. (Amended) A polypeptide pair comprising a first polypeptide immobilized to a support, and a second binding partner polypeptide bound to the first polypeptide, wherein

the binding of the polypeptides to each other is detectable, and

covalent modification of at least one of the polypeptides results in modulation of the binding, and is required for said association of said first polypeptide and said second binding partner polypeptide, wherein said covalent modification comprises one of the group consisting of phosphorylation, acylation, geranylation, glycosylation, ubiquitination, prenylation, sentrinization, ADP-ribosylation and the reversal of these covalent modifications.

21. (Amended) A method for detecting, in a sample, the presence of a modifying enzyme which covalently modifies a first polypeptide, the method comprising the steps of:

a) providing a first polypeptide immobilized on a support, wherein said first polypeptide comprises a binding site to which a second polypeptide specifically binds, and wherein covalent modification of said first polypeptide detectably changes the association of said first and second polypeptide;

b) providing said second polypeptide and said test sample, and contacting said second polypeptide and said test sample with said first polypeptide immobilized on a support;

c) measuring association of said first polypeptide with said second polypeptide; and

d) comparing said association with the association of a first and second polypeptide contacted with a control sample known to contain said modifying enzyme wherein a change in the association of said first and second polypeptide determined in step (c) relative to said association determined in step (d) provides an indicator of the presence of the enzyme in said test sample.

REMARKS

Claims 1-12, 14, 15, 17, 18, 20 and 21 are pending. Claims 13 and 16 are canceled herein. Claims 1, 17 and 21 are amended herein. The amendments are supported throughout the specification and add no new matter.

Applicants gratefully acknowledge the withdrawal of the prior rejections over Bronstein et al., Tsien et al., Lakowicz et al., Gallatin et al., and Sehr by the Examiner.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-18, 20 and 21 are rejected under 35 U.S.C. §112, second paragraph as indefinite.

Claim 1 is said to be indefinite for recitation of the term "enzyme" while none of the methods steps detect the presence of the enzyme in the sample defined in the preamble of the claim. Applicants submit that the amendment of the body of claim 1 to recite "whereby the presence of a modifying enzyme is detected" is sufficient to overcome this ground of rejection.

Claim 1 is said to be indefinite for recitation of the phrase in subsection (c) "the immobilized polypeptide with the second polypeptide." The Office Action asks, "In light of no second polypeptide having been provided, what is the second polypeptide?" Applicants submit that the amendment of claim 1 to recite "a polypeptide pair comprising a first polypeptide and a *second* binding partner polypeptide capable of associating" is sufficient to overcome this ground